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The Path to Human Clinical Trials

Introduction

- We have entered Phase III.
- We intend to begin human clinical trials in 2025.
- This presentation outlines the objectives for achieving this ultimate goal.

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Objectives

- Stage I - Preclinical
  - Publish Animal Trials Report + Histology Studies
  - Decellularization Protocol Refinement
  - Recellularization Protocol Refinement
- Stage II - Preclinical
  - The Surgical Protocol
  - CRO Selection
  - Regulatory Inquiry
- Stage III - Human Clinical Trials
  - Milestones Management
  - Cross-Functional Coordination
  - Risk Management and Contingency Planning
  - Documentation and Communication

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The Path to Human Clinical Trials

Animal Trials Report + HistologiX Data

- **Action:** Foregen must obtain the full report, requisite data, and supporting documentation from the rat and sheep trials conducted at the University of Camerino and the histology study conducted by HistologiX.
- **Clarification:** Ensure that the data is complete (including raw data, analysis, and ethical approvals). The animal trials report must be included in the application package for ethics approval in the human clinical trials (HCTs).
- **Next Step:** Once the report is obtained, integrate it into the RA/EC (regulatory authority/ Ethics Committee) submission for approval before proceeding with HCTs.

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The Surgical Plan

- **Action:** The Chief Medical Officer (CMO) will develop a comprehensive surgical plan outlining the procedure and safety measures. This surgical plan will be translated into a **protocol** by the Contract Research Organization (CRO) and used as the foundation for the HCTs. The protocol will need to be submitted to the appropriate regulatory authorities.
- **Process:** The CMO will create a surgical plan detailing the procedure. The CRO will translate it into a protocol and develop the trial design, objectives, and safety monitoring.

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Regulatory Inquiry Based on the CMO's Protocol (1/3)

- **Action:** Based on the finalized protocol, we will need to turn to the relevant regulatory authority and seek Scientific Advice or Pre-Submission Guidance to determine the appropriate submission category and requirements for approval.

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Regulatory Inquiry Based on the CMO's Protocol (2/3)

- **Regulatory Categories to Be Determined:** The regulatory authority (e.g., FDA, EMA, MHRA, Health Canada, PMDA) will help determine under which category the protocol should be classified. These categories may include but are not limited to:
  - Surgical Method: If the project is a procedure-based intervention.
  - Medical Device: If the project involves equipment like a bioreactor, it may fall under the IDE category.
  - Biologic: If the protocol involves biologically-derived materials like extracellular matrix (ECM), it may need to be submitted under the IND process.
  - Tissue Engineering: If the project involves tissue regeneration or engineering, it could fall under tissue-engineering product guidelines.
  - Combination Product: If both a device and biologic are involved (e.g., a bioreactor and ECM), the product may be classified as a combination product.
  - Advanced Therapy Medicinal Product (ATMP): For the EMA, the project may be classified as an ATMP if it involves tissue-engineered products or gene therapy.
  - Regenerative Medicine: If the project is regenerative in nature, it may follow pathways for regenerative medicine, such as those offered by Japan's PMDA.

Regulatory Inquiry Based on the CMO's Protocol (3/3)

- **Scientific Advice Procedure:** During the Scientific Advice or Pre-Submission Meeting, the regulatory authority will:
  1. **Classify the Project:** Confirm whether the protocol falls under surgical method, medical device, biologic, tissue engineering, or combination product categories.
  2. **Advise on Submission:** Clarify under which regulatory framework the protocol must be submitted (e.g., IND, IDE, ATMP), including the exact documentation and requirements.
  3. **Provide Guidance on Study Setup:** Offer insights on how the human clinical trial should be designed, covering:
     - **Study Design:** Appropriate trial phases (Phase I, II, or III), study structure (randomized controlled trials, etc.).
     - **Endpoints:** Key clinical outcomes to measure (e.g., safety, efficacy, patient function).
     - **Patient Population:** Recommendations on inclusion/exclusion criteria, sample size, and patient demographics.
     - **Risk Management:** Expectations for managing risks and adverse events during the study.
     - Etc.
  4. **Regulatory Pathway:** Outline additional steps if the project falls under more than one regulatory category (e.g., biologic and device), and whether harmonization between different regulatory agencies is possible.

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Selecting a CRO

Selecting a Contract Research Organization (CRO) (1/2)

- **Action:** After obtaining Scientific Advice and determining the exact regulatory requirements, the next step is to select a CRO. The CRO will play a key role in:
  - **Protocol Development:** Based on the CMO's preliminary protocol and the guidance received from Scientific Advice, the CRO will:
    - Propose a detailed study setup, including trial design, patient population, endpoints, and methodology.
    - Develop the full HCT protocol incorporating regulatory and scientific advice.
  - **Submission Preparation:** The CRO will assist in preparing the Clinical Trial Documentation (CTD) for submission to the relevant regulatory authorities.
  - **Conducting the HCT:** Once the protocol is approved, the CRO will conduct the HCT as per the finalized protocol.

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Selecting a Contract Research Organization (CRO) (2/2)

- Selection Criteria:
  - Region of Submission: The CRO should have expertise in the regulatory framework of the region where the clinical trial documentation (CTD) will be submitted. This could be:
    - **FDA** for the USA.
    - **EMA** for the EU.
    - **MHRA** for the U.K.
    - **PMDA** for Japan.
    - **Health Canada** for Canada.
    - **Developing countries** for regions where medical tourism may be pursued.
  - **Expertise:** The CRO must have specialized knowledge in the type of product being tested (e.g., device, biologic, or combination product) and experience in writing protocols according to the specific requirements of the relevant regulatory authority.
  - **Budget Constraints**: The CRO's pricing structure must align with the project's financial capabilities.
  - **Ethics Approval:** The ease and speed with which the CRO can obtain ethics approval in the chosen region is another key factor.
  - **Trial Execution Experience**: The CRO's experience in successfully managing clinical trials for similar products or procedures is essential to ensure quality and compliance.

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Selecting a Contract Research Organization (CRO) (2/2)

- **Impact on Study Design:** The choice of CRO will influence the detailed design of the study, including trial phases, patient population, endpoints, and risk management strategies.

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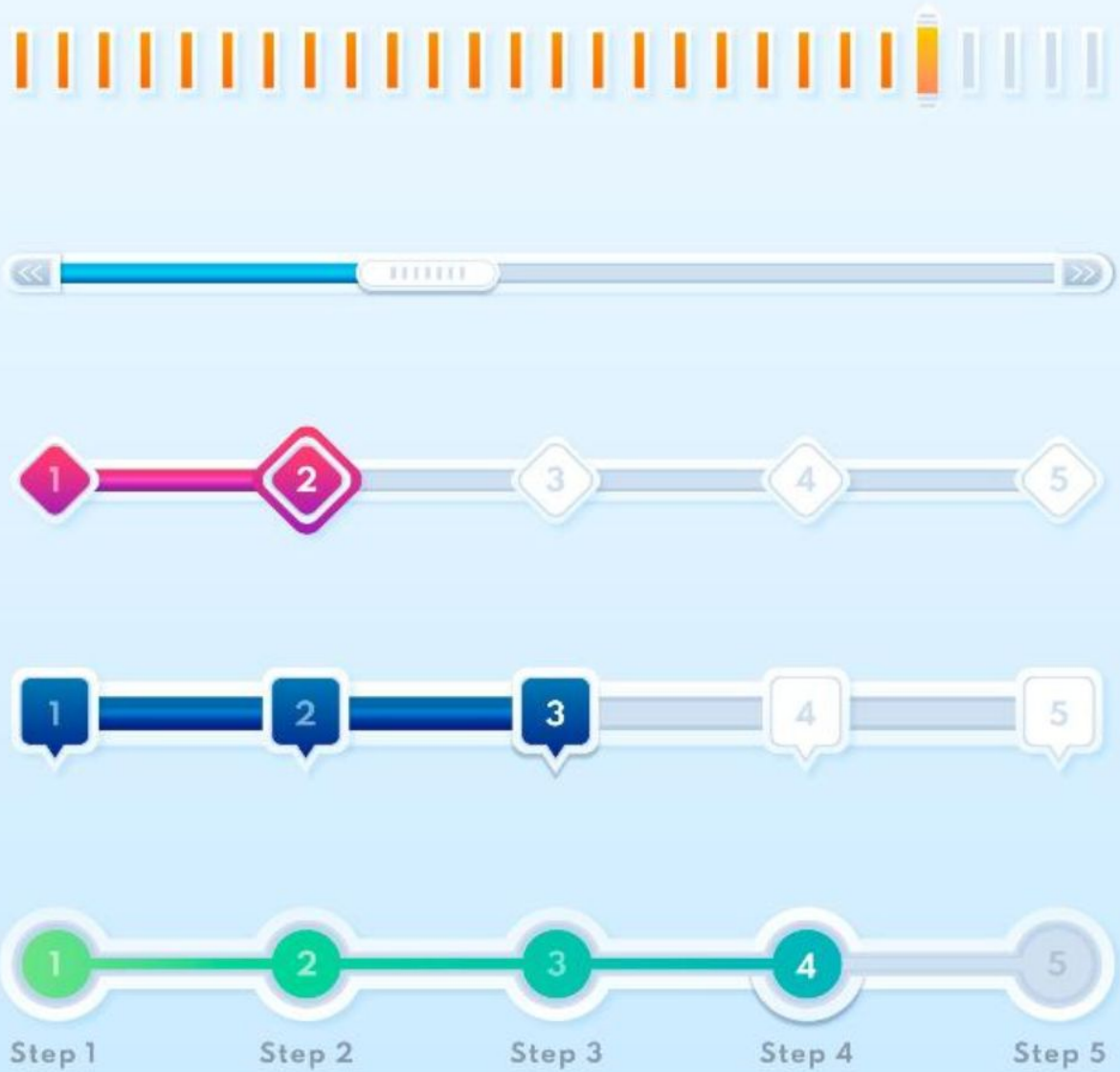
Milestones Management



Milestones Management

- **Action**: Develop a detailed project timeline to ensure all milestones are met efficiently. Key components of the timeline should include:
  - **Animal Trials Report**: Schedule and track the acquisition and integration of animal trials report and data into the application package for ethics approval.
  - **Protocol Development**: Complete HistologiX study. Plan the timeline for drafting, reviewing, and finalizing the HCT protocol, including incorporating feedback from the Scientific Advice.
  - **CRO Selection and Setup**: Include milestones for selecting a CRO, reviewing their study setup proposals, and finalizing contracts.
  - **Regulatory Submissions:** Allocate time for preparing and submitting Clinical Trial Documentation (CTD) to regulatory authorities, ensuring all documentation meets regulatory requirements and deadlines.
  - **Ethics Approval:** Factor in the time required for obtaining ethics committee approval before initiating the HCTs.- Parallel with RA.
  - **Study Execution:** Outline the timeline for conducting the HCTs, including patient recruitment, monitoring, and data collection.
- **Objective:** Ensure that the project adheres to the established schedule to avoid delays and maintain alignment with overall project goals.

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Cross-Functional Coordination

- **Action:** Regular and effective coordination between all functional teams involved in the project, including:
  - **Legal Team:** Work closely with the legal team to ensure that all regulatory and contractual requirements are met, including intellectual property considerations and compliance with international regulations.
  - **Regulatory Team:** Coordinate with the regulatory team to ensure that all submissions, approvals, and correspondence with regulatory authorities are managed effectively.
  - **Clinical Team:** Collaborate with the clinical team to ensure that the protocol and study design are feasible and aligned with clinical objectives and patient safety requirements.
  - **CRO:** Maintain ongoing communication with the CRO to ensure that protocol development, study setup, and execution are aligned with regulatory expectations and project goals.
- **Objective:** Achieve seamless integration of efforts across teams to address any issues promptly, ensure regulatory compliance, and support successful project execution.

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Risk Management and Contingency Planning

- **Action:** Identify potential risks and develop contingency plans to mitigate them. Key risks and their mitigations include:
  - **CMO-Related Delays:** Address potential delays in receiving the CMO's protocol or input. Implement a timeline buffer for protocol development and maintain open communication channels with the CMO to expedite the process.
  - **Regulatory Delays:** Develop strategies to address potential delays in regulatory approvals or protocol modifications. Plan for additional time and resources if regulatory feedback requires significant changes.
  - **Ethics Committee Feedback:** Prepare for potential revisions based on ethics committee feedback and ensure quick turnaround times to avoid extended delays.
  - **CRO Performance:** Monitor CRO performance closely and have contingency plans for switching CROs if necessary to ensure that the study progresses without interruption.
- **Objective**: Minimize the impact of unforeseen issues on the project timeline and ensure that there are proactive measures in place to handle potential challenges effectively.

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Documentation and Communication

- **Action:** Maintain thorough documentation of all project activities and decisions. Ensure effective communication channels are established between functional teams and stakeholders.
  - **Documentation:** Keep records of all correspondence, draft and finalize documents, protocols, regulatory submissions, approvals, and decisions with stakeholders.
  - **Communication:** Implement regular project updates and meetings to keep all team members informed and aligned.
- **Objective:** Ensure transparency and accountability throughout the project, facilitating smooth coordination and decision-making.

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Here’s to a successful Phase III!

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